DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

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DEC 16 2002

Don Jantzen
Director, Regulatory Affairs
Pfizer Consumer Healthcare
170 Tabor Road
Morris Plains, New Jersey 07950

RE: Docket Nos. 80N-0042/PR4 and 81N-0033/PR8

Dear Mr. Jantzen:

This letter responds to your revised 6-month gingivitis study protocol dated October 14, 2002 and filed under Docket No. 80N-0042 (as PR4) and Docket No. 81N-0033 (as PR8).

The Division of Over-the-Counter Drug Products, in cooperation with the Division of Dermatologic and Dental Drug Products, has the following comments:

1. The trial as designed should be able to determine if Listerine with fluoride (EOF) is as effective as Listerine (EO) in reducing gingivitis and plaque. The results of this study, in combination with the demonstration of the effectiveness of the fluoride component, will determine if EOF can be a monographed product. We will explore regulatory mechanisms for interim marketing under the OTC drug monograph procedures at that time.

2. The magnitude of difference between the placebo and both EO and EOF will be useful in the determination of inclusion of both products in a final monograph. The standard applied to antigingivitis drug products approved under NDAs is also applicable to monographed antigingivitis drug products, and that is a 20% difference between active therapies and control.

3. EO is currently labeled for use in individuals ages 12 and above. The inclusion criteria in this proposed protocol should include subjects between the ages of 12 and 18, significantly weighted at the low end of this age range.

4. The protocol states that a sufficient number of subjects will be enrolled to ensure that 340 subjects complete the study (page 2 of the protocol). Please provide information on the total number of patients planned to be enrolled, as all subjects enrolled in the study and dispensed test materials would be included in the intent-to-treat (ITT) population for efficacy analysis.

5. The method used to assign treatment to enrolled subjects based on smoking status (i.e., from the smallest number vs. from the highest number) is not clearly defined. For randomization based on a stratification factor, subjects should be randomized to received one of the three treatments within

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each stratum. The protocol should specify how subjects are randomized within each stratum, including block size, if any.

6. For non-inferiority comparison, both ITT and per-protocol (PP or evaluable) analyses are recommended to assess the consistency of efficacy results. The protocol should pre-specify the criteria for subjects to be included in the PP population. Please propose method(s) for handling missing data, as statistical analysis for the ITT population would be carried out based on all randomized subjects who are dispensed study materials.

7. The proposed analysis for the primary and the secondary efficacy endpoints based on the ANCOVA method is acceptable. It is recommended that interaction effect be tested at a significance level of 0.10 instead of 0.05.

Any comments you wish to provide on the above information should be submitted in triplicate, identified with the docket and comment numbers at the top of this letter, to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852.

We hope this information will be helpful.

Sincerely yours,

Charles J. Ganley, M.D.
Director
Division of OTC Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

AAC Consulting Group, Inc.
Information Services Division

January 15, 2003

10644
Chris Moorman
U.S. Oral Products
PROCTER & GAMBLE COMPANY
8700 Mason-Montgomery Road
Mason, OH 45040

Dear Chris Moorman:

In response to your request of 1/15/2003 enclosed is the following:

Per your standing request for information pertaining to monitored docket 81N-0033, enclosed is a letter sent from FDA to Pfizer.

If we can be of further assistance, please let us know.

Sincerely,

Virginia Smith
Research Associate

Enclosure

Please reference our control number 80373 when inquiring about this request.